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Case Report

# Sequential transition of mid-basilar variant to apical form of Takotsubo syndrome

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ABSTRACT

Takotsubo syndrome, also called apical ballooning syndrome, is a clinical entity characterized by transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid and apical segments without flow limiting obstructive coronary lesions. There have been many reported morphologic variants of apical ballooning syndrome based upon distribution of segment involvement including traditional apical, midventricular, and basilar. We present a patient who demonstrated sequential transition of mid-basilar type to classical apical ballooning type.

<**Learning objective:** Takotsubo syndrome mimics acute coronary syndrome and is accompanied by reversible left ventricular apical ballooning in the absence of angiographically significant coronary artery stenosis. Many morphological presentations can present, hence increased awareness may help practitioners identify and properly treat this condition. This is the first reported case of a sequential transition between variants.>

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## Introduction

A rare left ventricular (LV) apical wall motion abnormality was first described by Sato et al. [1], who later named this new condition as "Takotsubo"-shaped cardiomyopathy because the LV shape on angiogram resembled the shape of a *tako-tsubo* or a Japanese octopus pot. Takotsubo syndrome, also known as transient LV apical ballooning syndrome, stress-induced cardiomyopathy, broken heart syndrome, or ampulla cardiomyopathy [2] is now a well-recognized entity. Often, presentation of this condition mimics acute coronary syndrome with akinesia of the apical, basal, and/or mid portions of the left ventricle without significant coronary artery stenosis. There have been many reported morphologic variants of Takotsubo syndrome based upon distribution of segment involvement including traditional apical, midventricular, and basilar. We present the first reported case of a patient with sequential transition of a mid-basilar type to traditional apical ballooning type during the same admission without complete recovery in between.

## Case presentation

A 39-year-old Caucasian female patient with a history of depression, and alcohol and drug abuse was admitted on August 9th 2005 to Saint Mary's Hospital in Rochester, Minnesota for dyspnea for approximately 12 h. Twelve weeks prior to the Emergency Department (ED) visit, the patient underwent a cesarean section without any complications. On current admission in the ED, a computed tomography scan of the chest revealed no pulmonary embolism, but showed a focal consolidation in the superior segment of the left lower lobe with lesser infiltrates in the remainder of the left lower lobe consistent with pneumonitis. An initial electrocardiogram (ECG) was performed showing sinus tachycardia and non-specific ST abnormalities (Fig. 1). Initial cardiac biomarkers revealed a troponin-I of 0.25 μg/L and brain natriuretic peptide of 355 pg/ml. White blood count (WBC) was $25.2 \times 10^3/\mu l$, while erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were 16 mm/h and 0.9 mg/L respectively. Vital signs on exam revealed tachycardia at a rate of 115 beats per minute, blood pressure of 103/69 mmHg, respiratory rate at 24 breaths per minute, and oxygen saturation of 88% on room air. On examination, the patient appeared to be in mild respiratory distress. Physical exam was otherwise unremarkable except for decreased breath sounds on the left with crackles appreciated at the middle and lower lung fields. An albuterol nebulizer was initiated, but the patient's saturations continued to drop into the lower 70 s; therefore the patient was transferred to the medical intensive care unit (MICU). In the MICU, an initial echocardiogram performed on August 9th revealed severe hypokinesis to akinesis of the mid and basal segments of the LV with preserved contractility of the apical segments (Figs. 2 and 3). Estimated LV ejection fraction was 23%. Regional wall motion abnormalities (RWMA) illustrated mid and basal variant forms of Takotsubo syndrome. The patient continued to remain on oxygen after one week and further laboratory testing revealed a troponin-I of 0.16 μg/L. An ECG at that time revealed normal sinus

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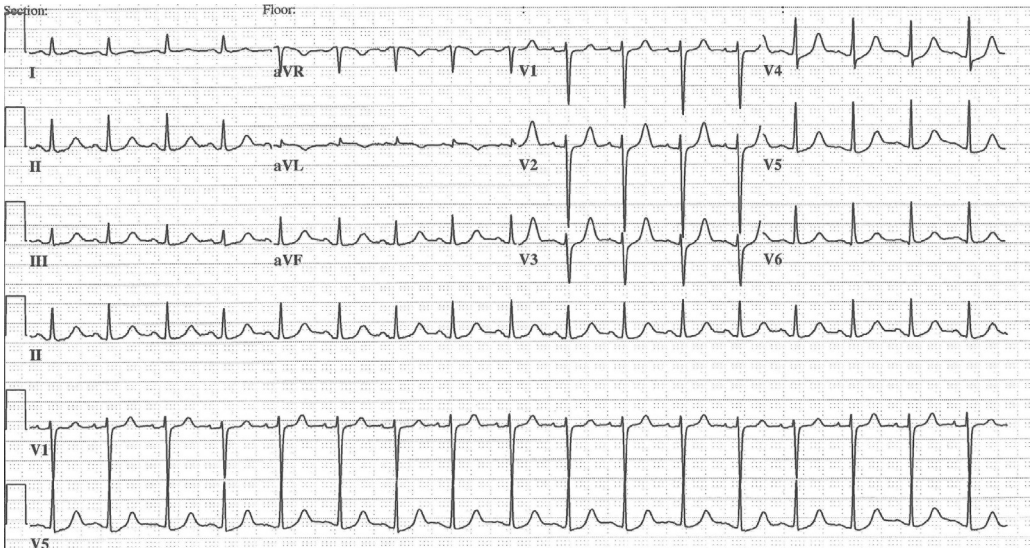


**Fig. 1.** Admission electrocardiogram showing sinus tachycardia and non-specific ST abnormalities.

rhythm with T-wave flattening and Q-waves present in the anterolateral leads (Fig. 4). A subsequent echocardiogram (Figs. 5 and 6) performed on the 16th of August revealed reversal of the RWMA, namely, complete recovery of the contractility of the basal and mid segments and severe hypokinesis of the apical segments compared to the echocardiogram a week prior. In this instance, the typical form of Takotsubo syndrome was present. The patient subsequently had a cardiac catheterization performed given ECG and imaging findings, which showed no significant luminal stenosis of greater than 50% nor evidence of vasospasm by acetylcholine provocation test. The patient clinically improved and repeat ECG on discharge showed normal sinus rhythm with some mild T-wave flattening in leads V1–V2 (Fig. 7). The patient was sent to a skilled nursing facility on August 19th and was to be followed by her local physicians.

## Discussion

Takotsubo syndrome is classically defined as symmetric severe hypokinesia or akinesia of the left ventricular wall of the mid and especially the apical segments with or without hyperdynamic function of the base. On the other hand, a "reciprocal" form of this syndrome is also present where the apex is hyperkinetic while the base is hypokinetic or akinetic. Another form of Takotsubo syndrome involving only the mid-ventricle has also been described. In this condition, the apical and basal segments are both either normokinetic or hyperkinetic. While many forms of Takotsubo syndrome exist [3–9], the basis of the presentation, clinical features, and the transient nature of the condition in all suggests a shared pathophysiological etiology to some extent [10]. Some reports state that the abnormal wall motion normalized within 17.4

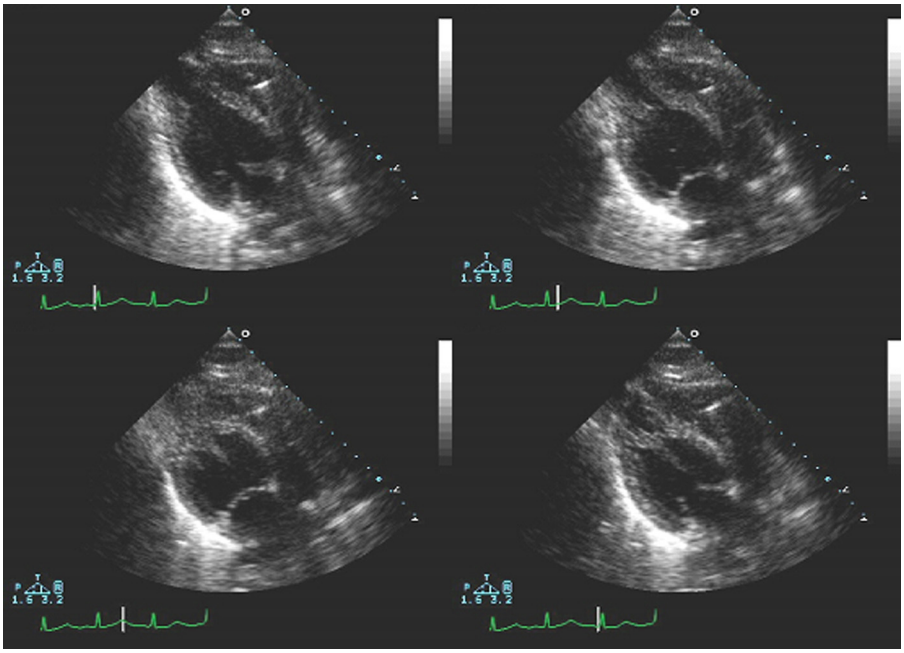

**Fig. 2.** Initial echocardiograph revealing generalized severe hypokinesis to akinesis with function best preserved in the mildly hypokinetic apical segments. Regional wall motion abnormalities illustrated mid variant form of apical ballooning.

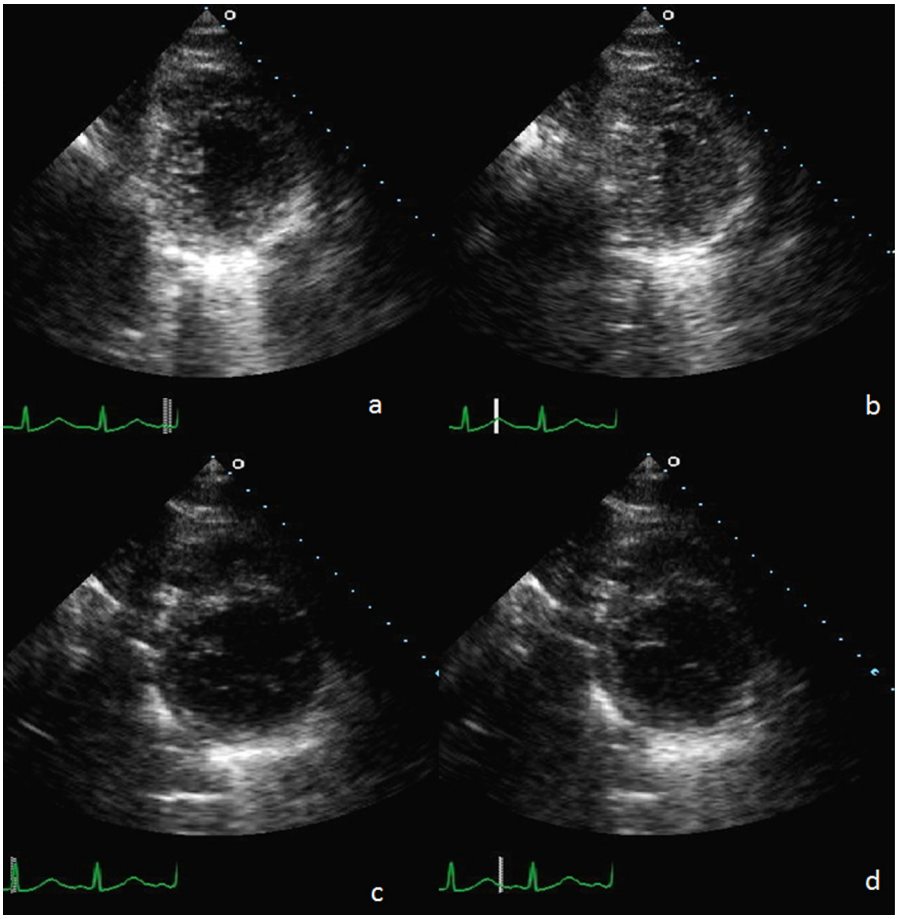


**Fig. 3.** Initial echocardiograph: (a) basal short axis in diastole and (b) systole images demonstrate severe hypokinesis of the basal LV segments. (c) Apical short axis diastolic and (d) systolic images demonstrate significant change in the LV dimensions indicating hyperdynamic contractility of the LV apical segments.

days [11]. During the akinetic state, LV ejection fraction is significantly impaired from estimates anywhere between 15 and 40% with mean of 29% [12].

While first emerging in the Japanese population, Takotsubo syndrome has now been seen in Caucasian populations throughout the USA [13]. In addition, almost 90% of reported patients are female and the majority are post-menopausal or above 50 years of age. Prognosis is generally favorable in the short-term, yet no long-term outcome studies are currently available.

Takotsubo syndrome is frequently diagnosed as an acute coronary syndrome, because cardiac biomarker levels are frequently

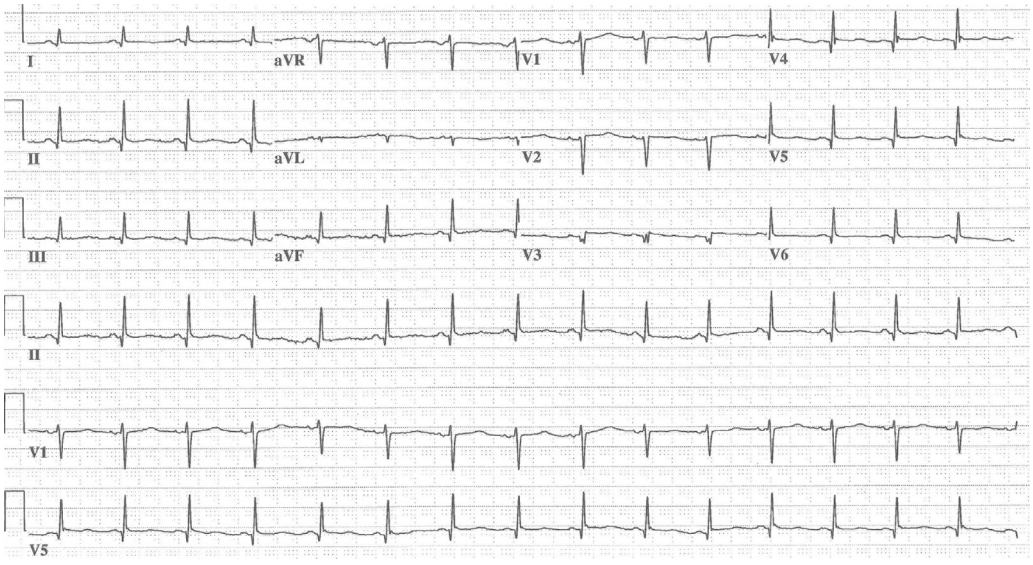


**Fig. 4.** Subsequent electrocardiogram showing normal sinus rhythm with T-wave flattening and Q-waves present in the anterolateral leads.

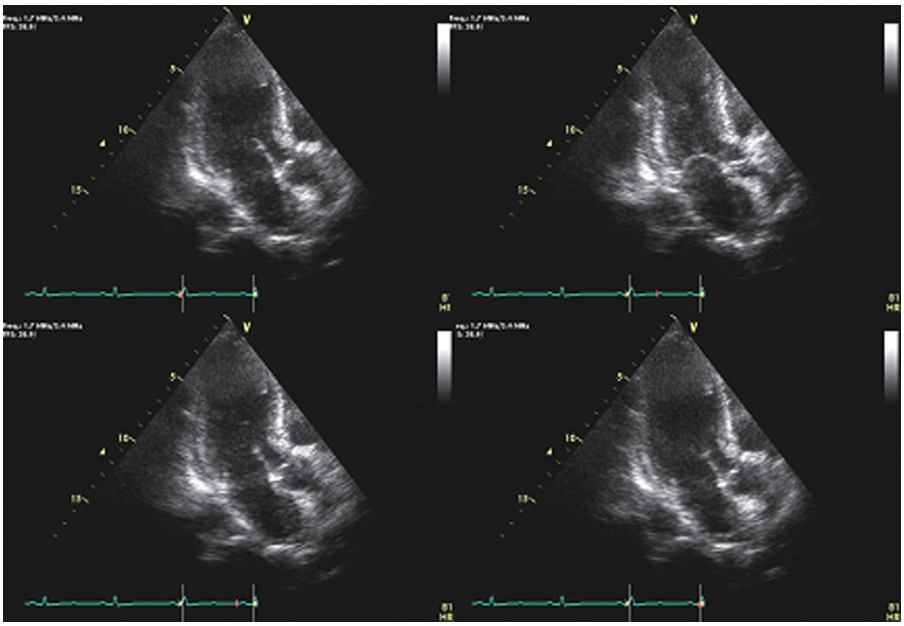

**Fig. 5.** Second echocardiograph one week later showing typical form of apical ballooning was present in which the entire apical segments were akinetic.

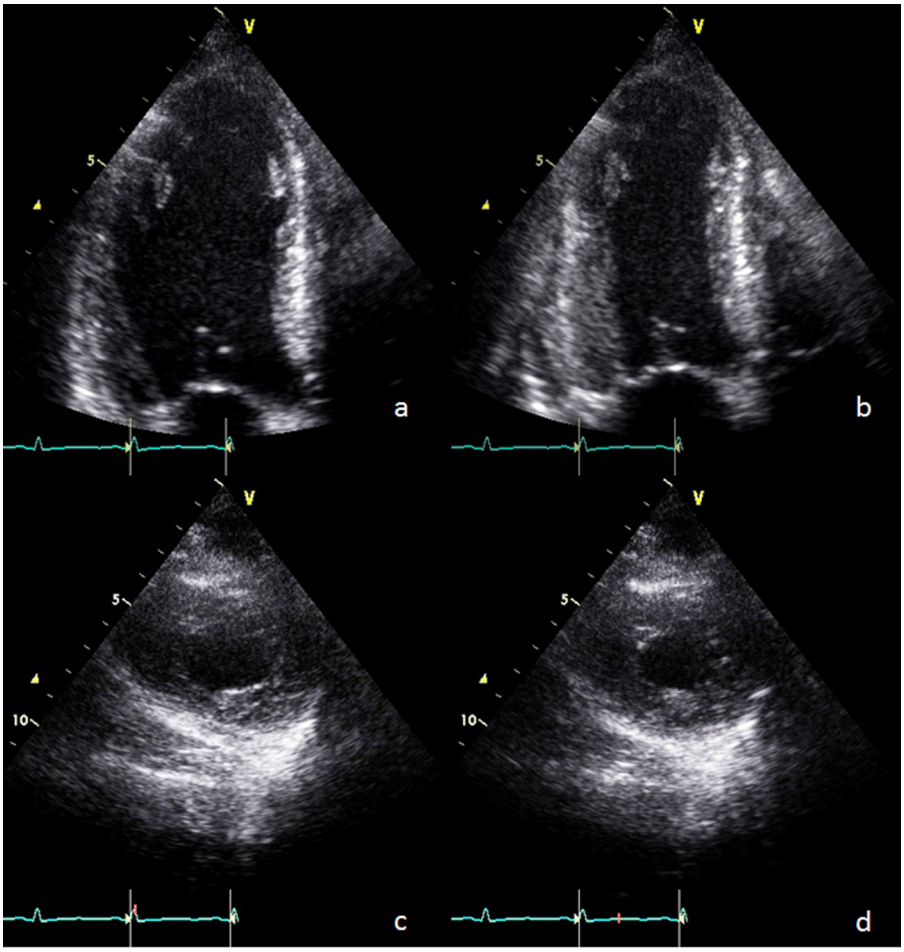


**Fig. 6.** Second echocardiograph: (a) apical 4 chamber echo images diastole and (b) systole demonstrates akinetic to dyskinetic apex while basal left ventricular (LV) demonstrates systolic change in LV dimension. (c) Apical short axis images demonstrate no change in LV apical dimension from diastole to (d) systole indicating apical akinesis.

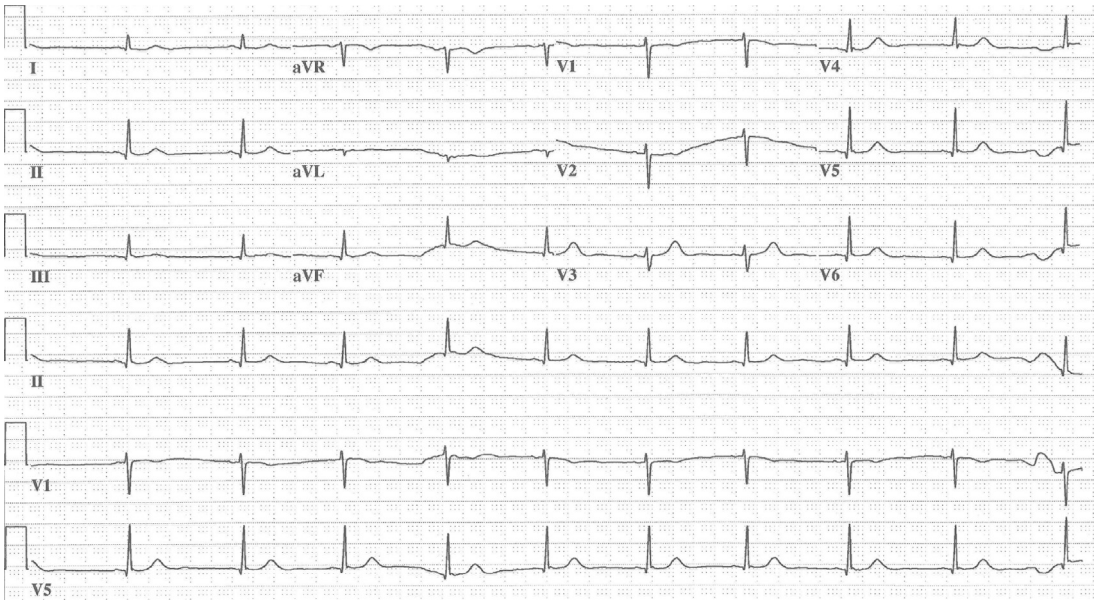


**Fig. 7.** Pre-discharge electrocardiogram showing normal sinus rhythm with some mild T-wave flattening in leads V1–V2.

raised, mimicking acute myocardial infarction and LV function is impaired with regional wall-motion abnormalities. Coronary angiography is required to make the diagnosis of Takotsubo syndrome. Coronary angiography usually reveals mild abnormalities that do not meet the definition of obstructive coronary lesions (>50% luminal stenosis), as was the case in our patient. Furthermore, the akinetic zones do not correspond to a perfusion territory of a single coronary artery. Interestingly, the patient did develop ECG changes suggesting possible myocardial damage, however subsequent angiogram did not show evidence of coronary disease. These ECG findings also resolved prior to discharge, proposing the possibility of non-infarction or transient Q-waves, which may be explained by her underlying hypoxia. Additionally, transient Q-waves have been reported with other instances of Takotsubo syndrome [14]. Additionally, ESR and CRP markers were also low on admission, leading less to the possibility of myocarditis.

Multiple theories about the pathophysiological mechanism of this condition are present, yet none has sufficient compelling evidence. Possible theories such as catecholamine-mediated multivessel epicardial spasm [15], microvascular coronary spasm [16], impaired fatty acid metabolism [17], possible direct catecholamine-mediated myocyte injury [18], or reduced estrogens have been advocated [19,20].

Cerebrovascular insults, such as subarachnoid hemorrhage, have also been implicated in causing transient RWMA [21,22]. The proposed mechanism is once again an excess catecholamine surge, similar to Takotsubo syndrome, but differs in that these processes tend to spare the apex and involve the basal segments. Although the pathophysiology is unknown, it is hypothesized that microvascular spasms and excessive release of catecholamines from myocardial sympathetic nerves may be the potential cause [1]. A recent pooled analysis by Guglin and Novotorova [23] illustrates that neurogenic stunned myocardium and Takotsubo syndrome may be in the same spectrum of disease. Recently, Lyon et al. [24] hypothesized the cellular mechanism in which high levels of circulating epinephrine trigger a switch in intracellular signal trafficking in ventricular cardiomyocytes, from Gs protein to Gi protein signaling via the β2-adrenoceptor, where a negative inotropic outcome results from the intense activation of receptors. In addition, this negative inotropic effect is greatest at the apical myocardium, in which the β-adrenoceptor density is greatest. Our case demonstrates a unique phenomenon where in at the time of presentation, the basal and mid ventricular myocardial segments were involved with sparing of the apex and subsequently the apex was stunned with total recovery of the basal and mid ventricular segments a few days later. Chattopadhyay and John [25] reported a patient who had sustained a subarachnoid hemorrhage and initially presented with an apical ballooning pattern which, within a few hours, demonstrated recovery of the apex and involvement of the base. These two cases, as well as diverse presentations of stress-induced cardiomyopathy reported in the literature, suggest that in addition to enhanced sympathetic activity there is also "accentuated antagonism" [26]. Basal left ventricular myocardium is rich in muscarinic acetylcholine receptors and plays an important role in parasympathetic control of the heart [27]. Vagal stimulation has been shown to decrease the ventricular contractility independent of the effects on heart rate [28]. The vagal discharge at the sub cellular level increases cyclic GMP resulting in decreased contractility of the base of the left ventricle [29].

Although a myriad of atypical LV morphological presentations of Takotsubo syndrome have been reported in the literature in the past, we have come across a novel entity in which the two most common presenting forms are present in a single patient within days demonstrates the differences in the distribution of cardiac adrenoceptors, muscarinic receptors, and their interaction and evidence of accentuated antagonism. This information may help us to better understand the pathophysiology of this mysterious condition, which may inevitably help create possible therapeutic options.

## Conflict of interest

Authors declare no conflict of interest.

## References

[1] Sato H, Tateishi H, Uchida T, Dote K, Ishihara M, Sasaki K. Tako-tsubo-like left ventricular dysfunction due to multivessel coronary spasm. In: Kodama K, Haze K, Hori M, editors. Clinical aspect of myocardial injury: from ischemia to heart failure. Tokyo: Kagakuhyoronsha Publishing Co.; 1990. p. 56–64.

[2] Kawai S, Suzuki H, Yamaguchi H, Tanaka K, Sawada H, Aizawa T, Watanabe M, Tamura T, Umawatari K, Kawata M, Nakamura T, Yamanaka O, Okada R. Ampulla cardiomyopathy ('Takotusbo' cardiomyopathy) – reversible left ventricular dysfunction: with ST segment elevation. Jpn Circ J 2000;64:156–9.

[3] Yoshida T, Nishizawa T, Yajima K, Tsuruoka M, Fujimaki T, Oguri M, Kato K, Hibino T, Ohte N, Yokoi K, Kimura G. A rare case of tako-tsubo cardiomyopathy with variable forms of left ventricular dysfunction: a new entity. Int J Cardiol 2009;134:e73–5.
[4] Karavidas A, Arapi S, Fotiadis J, Zacharoulis A, Matsakas E. A variant form of acute reversible cardiomyopathy: a case report. J Med Case Rep 2008;2:74.
[5] Cacciotti L, Camastra GS, Beni S, Giannantoni P, Musarò S, Proietti I, De Angelis L, Semeraro R, Ansalone G. A new variant of Tako-tsubo cardiomyopathy: transient mid-ventricular ballooning. J Cardiovasc Med (Hagerstown) 2007;8:1052–4.
[6] Fazio G, Novo G, Azzarelli S, Evola S, Barbaro G, Sutera L, Di Gesaro G, Akashi YJ, Novo S. Transient mid-ventricular dyskinesia: a variant of Takotsubo syndrome. Int J Cardiol 2008;129:272–3.
[7] Nanda S, Pamula J, Bhatt SP, Chan I, Turki MA, Dale TH. Takotsubo cardiomyopathy – a new variant and widening disease spectrum. Int J Cardiol 2007;120:e34–6.
[8] Mazzarotto P, Stecconi P, Gemelli F, Azzarito M, Farnetti F. A case of ballooning syndrome with atypical anterior localization. Ital Heart J Suppl 2005;6:730–4.
[9] Haghi D, Papavassiliu T, Flüchter S, Kaden JJ, Pörner T, Borggrefe M, Suselbeck T. Variant form of the acute apical ballooning syndrome (takotsubo cardiomyopathy): observations on a novel entity. Heart 2006;92:392–4.
[10] Hurst RT, Askew JW, Reuss CS, Lee RW, Sweeney JP, Fortuin FD, Oh JK, Tajik AJ. Transient midventricular ballooning syndrome: a new variant. J Am Coll Cardiol 2006;48:579–83.
[11] Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Koike H, Sasaka K. The clinical features of takotsubo cardiomyopathy. QJM 2003;96:563–73.
[12] Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, Maron BJ. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation 2005;111:472–9.
[13] Desmet WJ, Adriaenssens BF, Dens JA. Apical ballooning of the left ventricle: first series in white patients. Heart 2003;89:1027–31.
[14] Thakar S, Chandra P, Hollander G, Lichstein E. Electrocardiographic changes in Takotsubo cardiomyopathy. Pacing Clin Electrophysiol 2011;34:1278–82.
[15] Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakamura S, Yoshida M, Mitsuba N, Hata T, Sato H. Time course of electrocardiographic changes in patients with tako-tsubo syndrome: comparison with acute myocardial infarction with minimal enzymatic release. Circ J 2004;68:77–81.
[16] Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. J Am Coll Cardiol 2003;41:737–42.
[17] Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539–48.
[18] Mann DL, Kent RL, Parsons B, Cooper 4th G. Adrenergic effects on the biology of the adult mammalian cardiocyte. Circulation 1992;85:790–804.
[19] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008;155:408–17.
[20] Ueyama T, Hano T, Kasamatsu K, Yamamoto K, Tsuruo Y, Nishio I. Estrogen attenuates the emotional stress-induced cardiac responses in the animal model of Tako-tsubo (Ampulla) cardiomyopathy. J Cardiovasc Pharmacol 2003;42(Suppl. 1):S117–9.
[21] Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. J Am Coll Cardiol 1994;24:636–40.
[22] Zaroff JG, Rordorf GA, Ogilvy CS, Picard MH. Regional patterns of left ventricular systolic dysfunction after subarachnoid hemorrhage: evidence for neurally mediated cardiac injury. J Am Soc Echocardiogr 2000;13:774–9.
[23] Guglin M, Novotorova I. Neurogenic stunned myocardium and takotsubo cardiomyopathy are the same syndrome: a pooled analysis. Congest Heart Fail 2011;17:127–32.
[24] Lyon AR, Rees PS, Prasad S, Poole-Wilson PA, Stress Harding SE. (Takotsubo) cardiomyopathy – a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. Nat Clin Pract Cardiovasc Med 2008;5:22–9.
[25] Chattopadhyay S, John J. Tako-Tsubo and reverse Tako-Tsubo cardiomyopathy: temporal evolution of the same disease? Eur Heart J 2009;30:2837.
[26] Levy MN. Sympathetic–parasympathetic interactions in the heart. Circ Res 1971;29:437–45.
[27] Wang Z, Shi H, Wang H. Functional M3 muscarinic acetylcholine receptors in mammalian hearts. Br J Pharmacol 2004;142:395–408.
[28] Lewis ME, Al-Khalidi AH, Bonser RS, Clutton-Brock T, Morton D, Paterson D, Townend JN, Coote JH. Vagus nerve stimulation decreases left ventricular contractility in vivo in the human and pig heart. J Physiol 2001;534:547–52.
[29] Watanabe AM, Besch Jr HR. Interaction between cyclic adenosine monophosphate and cyclic gunaosine monophosphate in guinea pig ventricular myocardium. Circ Res 1975;37:309–17.